OSIMERTINIB (Tagrisso)

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (OSI1) (OSI2) (OSI3) (OSI5)

1. Osimertinib monotherapy for the first line treatment of locally advanced or metastatic epidermal growth factor receptor mutation-positive non-small cell lung cancer in adults. Has not received any previous cytotoxic chemotherapy or immunotherapy for the locally advanced/metastatic disease indication and has had no prior treatment with an EGFR inhibitor unless osimertinib has been received as adjuvant treatment for resected stages IB to N2 only IIIB NSCLC with either an EGFR exon 19 deletion or exon 21 substitution mutation and the patient did not progress whilst still receiving adjuvant osimertinib. PS 0 or 1. (TA654)
2. Osimertinib monotherapy for the second-line treatment of locally advanced or metastatic epidermal growth factor receptor T790M mutation-positive non small cell lung cancer in adults. There is at least evidence of radiological disease progression on 1st line EGFR-targeted tyrosine kinase (TKI) therapy and there has been no further systemic anti-cancer treatment. Has had no prior treatment with osimertinib or osimertinib has been received as adjuvant treatment for resected stages IB to N2 only IIIB NSCLC with either an EGFR exon 19 deletion or exon 21 substitution mutation and the patient did not progress whilst still receiving adjuvant osimertinib. PS 0 or 1. (TA653)
3. Osimertinib monotherapy for adjuvant treatment in adults after complete tumour resection in patients with UICC/AJCC 8th edition stage IB or stage IIA or stage IIB or stage IIIA or N2 only stage IIIB non-small cell lung cancer whose tumours have either an EGFR exon 19 deletion or an exon 21 (L858R) substitution mutation. Not received any pre-operative systemic therapy (cytotoxic chemotherapy, immunotherapy, no prior EGFR-targeted tyrosine kinase inhibitors) for the NSCLC.or any pre-operative or post-operative radiation therapy for the NSCLC. No more than 10 weeks have elapsed since surgery if the patient did not receive adjuvant chemotherapy or no more than 26 weeks have elapsed since surgery if the patient was treated with adjuvant cytotoxic chemotherapy after surgery for the NSCLC. PS 0 or 1. (TA1043)
4. Osimertininb monotherapy for treating EGFR mutation positive (exon 19 deletion (Ex19del) or an exon 21 (L858R) substitution mutation) unresectable locally advanced non-small cell lung cancer after two or more cycles of platinum-based chemoradiotherapy (but no prior treatment with an EGFR inhibitor) but no other prior systemic treatment. Has not progressed during or after platinum-based chemoradiotherapy.PS 0 or 1.

REGIMEN

OSIMERTINIB 80mg tablet orally once daily continuously

OSI5 will commence treatment with osimertinib no later than 6 weeks (42 days) after the last dose/fraction of minimum 2 cycles of chemotherapy/radiotherapy (whichever is the latter).

CYCLE FREQUENCY AND NUMBER OF CYCLES

Calendar years or months - maximum duration of treatment from initiation of the treatment, the treatment must stop at that maximum time duration irrespective of any breaks in treatment.

Adjuvant (OSI3) - until disease progression up to a maximum 3 **calendar** years.

Locally advanced, metastatic - until disease progression.

A formal medical review as to how osimertinib is being tolerated and whether treatment with osimertinib should continue or not will be scheduled to occur at least by the end of the second 4-weekly cycle of treatment.

ADMINISTRATION

Available as 40mg and 80mg tablets
Swallowed whole with water once daily With or without food
If the patient is unable to swallow the tablet, the tablet may first be dispersed in 50ml of non-carbonated water. It should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed. No other liquids should be added.

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Osimertinib	Some of the following may be required for treatment of the skin rash: E45 / Diprobase, Hydrocortisone 1%/2.5%, Clindamycin gel 1%, Oxytetracycline 500mg po bd (for 2 weeks) Prednisolone 25mg po od for 7 days then reducing by 5mg per day to stop. Diarrhoea – Loperamide may be required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle, may be less frequently once patients are stable
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥50
Chest x-ray
ECG at baseline, after 2 weeks of treatment and for patients with ongoing risk of other QT prolonging medication or cardiac failure
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Osimertinib	Skin rash – initial rash may be severe. If infected may require oral antibiotics Diarrhoea - dose reduction may be required. Moderate or severe diarrhoea may require loperamide Interstitial lung disease/pneumonitis Cardiomyopathy QTc interval prolongation

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Osimertinib	Strong CYP3A inducers eg rifampicin and clarithromycin should be avoided

DOSE MODIFICATIONS

Haematological

Osimertinib

If neutrophils <1.0x10^9/l or platelets <50x10^9/l, osimertinib should be interrupted until blood counts have recovered.

If counts recover within 3 weeks of stopping osimertinib, re-start treatment either at 80mg od or with a reduction to 40mg od.

If blood counts do not recover after 3 weeks, permanently discontinue.

Aplastic anaemia - discontinue permanently.

Non-haematological

Osimertinib

Cardiac

QTc interval >500msec on at least 2 separate occasions	Withold until interval <481 or recovery to baseline if baseline >481msec then resume at 40mg
QTC prolongation with signs/symptoms of life threatening arrhythmia	Discontinue permanently

Cutaneous

Stevens-Johnson syndrome - discontinue permanently

Other

Grade 3 or higher adverse reaction – withhold for up to 3 weeks

If improvement to grade 0-2 within 3 weeks - resume at 80mg or 40mg daily

If no improvement within 3 weeks - discontinue permanently

Pulmonary

Interstitial lung disease /pneumonitis - discontinue permanently

Hepatic impairment

Osimertinib

No dose adjustments are necessary in patients with mild hepatic impairment (Child Pugh A) or moderate hepatic impairment (Child Pugh B).

No dose adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤ULN and AST >ULN or total bilirubin >1.0-1.5xULN and any AST) or moderate hepatic impairment (total bilirubin 1.5-3xULN and any AST).

Use in patients with severe hepatic impairment is not recommended

Renal impairment

Osimertinib

Caution in severe renal impairment (CrCl <15ml/min) or end stage renal impairment.

REFERENCES

1. New England Journal Of Medicine Pasi A et all Vol 372 No 18 pages 1689-1699